Brown Tumour of the Maxilla – A Manifestation of Primary Hyperparathyroidism

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Abstract
In the past two decades, the practice of checking serum calcium on routine blood screens has led to earlier diagnosis of primary hyperparathyroidism. A case of brown tumour of the maxilla as the presenting symptom of primary hyperparathyroidism is presented.

Introduction
In the past two decades, the practice of checking serum calcium on routine blood screens has led to earlier diagnosis of primary hyperparathyroidism. It has become increasingly rare to find generalized osteoporosis, multiple focal areas of demineralization of the skull, or osteitis fibrosa cystica with brown tumour, as manifestations of the disease. It is especially rare for advanced bone disease, such as brown tumour, to present in the absence of other symptoms of hypercalcaemia. In addition, brown tumour involvement of the maxilla is itself quite uncommon. A case of brown tumour of the maxilla as the presenting symptom of primary hyperparathyroidism is presented.

Case Report
A 23-year-old man presented with a 2-month history of an enlarging mass beneath the right nasolabial fold. He had a history of a similar mass beneath the left nasolabial fold 6 months ago, which spontaneously decreased in size. He had a history of gradually increasing bilateral nasal obstruction since 6 months. The patient denied previous trauma, epistaxis or ocular changes. A complete review of systems was unremarkable, with absence of any symptoms of hypercalcaemia such as fatigue, malaise, joint pain, polyuria, or abdominal discomfort. However, the patient had a swelling of the right upper arm for which an orthopaedic reference was taken. The swelling was treated conservatively with a splint for about 8 weeks.

On examination, a 7-8 cm sized non-tender, immobile, smooth surfaced, hard mass was palpated beneath the right nasolabial fold. Another mass around 1 – 1.5 cm in size was palpated beneath the left nasolabial fold. Anterior rhinoscopy revealed a round, mucosal-covered mass extending along the floor and lateral wall of nose into the right nasal vestibule. No proptosis or extra-ocular muscle involvement was noted. Examination of the oral cavity revealed multiple swellings of the hard palate, more on the right side as compared to the left. Cervical adenopathy was not apparent.

A computed tomography scan of the paranasal sinuses demonstrated an expansile bony multiloculated lesion with severe osteolytic erosion and soft tissue density within, involving both the maxillae. The left maxillary lesion involved the floor of orbit with extension into the intra-orbital compartment. It also extended into the ethmoid air cells, inferior orbital fissure, infratemporal fossa, foramen ovale, sphenoid sinus and into the oral cavity. The right maxillary lesion extended into the infratemporal fossa, masticator space, the oral cavity and produced an outward bulge on the cheek, lip and orbit. Both the lesions extended centrally to completely obliterate the nasal cavity. The differential diagnosis included polyostotic type of fibrous dysplasia and brown tumour of hyperparathyroidism (Fig. 1).

A biopsy was taken from the right maxillary mass by sublabial approach, which was suggestive of brown
tumour of hyperparathyroidism.

Preoperative evaluation revealed elevated calcium at 12.83 mg/dL (normal: 8.5-11.0 mg/dL). Further investigation disclosed a parathyroid hormone value of 964 pg/mL (normal: 12-72 pg/mL).

An ultrasound of the neck showed a 1.5 x 0.7 cm, hypoechoic lesion postero-lateral to the right common carotid artery showing moderate vascularity; this lesion could represent a parathyroid gland adenoma.

A 99m Tc-Tetrofosmin scan revealed a parathyroid adenoma involving the inferior parathyroid gland on the right side.

A bone scan revealed multiple other areas of increased uptake involving the skull, spine, sternum, scapula, pelvis and both the femurs (Fig. 2).

The patient returned 20 days later for a right inferior parathyroidectomy. At surgery, the right inferior parathyroid gland was enlarged and the remainder of the parathyroid gland was normal to visual inspection. Hormone levels were done at induction (baseline levels), 10 minutes after removal of the tumour and 1 hour after tumour removal. The baseline levels at induction were 653 pg/ml. They fell dramatically 170 pg/ml to 10 minutes after tumour removal. The levels at 1 hour post-excision were 30.50 pg/ml. The patient has subsequently maintained normal parathyroid hormone and calcium levels over the last 2 years. The swellings on the face and palate have significantly reduced by more than 75%. The swelling of the upper arm has disappeared completely with no sequelae (Figs. 3 a and b).

Pathologic examination of the left inferior parathyroid gland revealed an encapsulated solid and cystic mass, 4.5 x 3.2 x 1.7 cm and weighing 7.97 g. Microscopically, the mass was composed of a cord-like growth of relatively uniform cells with round nucleoli and pale eosinophilic cytoplasm; intracytoplasmic fat was absent (Fig. 3). The pathologic findings along with the surgical findings were consistent with parathyroid adenoma. Pathologic examination of the maxillary tumour demonstrated a firm, brown, gritty mass, 3.0 x 2.7 x 1.7 cm. Microscopically, the centre of the lesion consisted of multinucleated giant cells and stromal cells; peripherally bone with osteoblastic and osteoclastic activity was present. Areas of haemorrhage and haemosiderin deposition were noted (Fig. 4).

Based on the pathologic and clinical findings, a diagnosis of brown tumour secondary to primary hyperparathyroidism was made. Postoperatively, the patient recovered without complication. Laboratory
analysis from both the immediate postoperative period and 1 year later revealed that the patient had attained both normal calcaemia and normal levels of parathyroid hormone. One year following the operation, a computed tomography scan exhibited no evidence of residual or recurrent maxillary tumour.

Discussion

Although primary hyperparathyroidism has a multitude of possible clinical presentations, it is becoming increasingly rare for the disease to present with only skeletal manifestations. In recent years, primary hyperparathyroidism has been most often diagnosed by elevated serum calcium on a routine or unrelated blood screen. In a 1980 study, 57% of 111 patients diagnosed with primary hyperparathyroidism had no symptoms of the disorder. In the same study, acute hypercalcaemic crisis (14%) and renal symptoms (7%), such as stones or infection, were more common presenting symptoms than were skeletal symptoms (4%), including osteopenia or brown tumour. Older studies had exhibited higher rates of skeletal involvement. In 1971, Wang found that 21% of 431 Massachusetts General patients with hyperparathyroidism had evidence of skeletal disease. The most frequent bone changes in primary hyperparathyroidism include diffuse subperiosteal bone resorption, loss of lamina dura of the teeth, and generalized osteoporosis. These changes are due to the increased calcium resorption from bone induced by the elevated levels of parathyroid hormone. For unknown reasons, certain focal areas of bone may undergo more extensive resorption, followed by a cellular repair process that results in the accumulation of fibrillar stroma and connective tissue cells along with multinucleated giant cells and spicules of osteoid deposition. In addition, haemorrhage and haemosiderin deposition occurs. This process results in the formation of a brown tumour. Brown tumours most commonly involve the ribs, clavicles, pelvic
girdle, and mandible. In a study of 220 patients with hyperparathyroidism, 4.5% had brown tumour of the mandible. Involvement of the maxilla, however, is very rare. In reported cases of brown tumour of the maxilla, patients all had additional manifestations associated with hyperparathyroidism, such as nephrolithiasis, fatigue and weakness, nausea and bone pain, hypertension, and polydipsia and polyuria. In addition, the presence of a brown tumour is nearly always associated with radiographic evidence of more generalized bone disease. Diagnosis of hyperparathyroidism and brown tumour should be considered in any patient with hypercalcaemia and a destructive and expansile bone mass. Radiographically, brown tumours appear as well-defined lytic lesions of the bone. The pathologically similar giant cell tumours often have indistinct borders and blend into the normal bone, a finding that may serve to distinguish them from brown tumours. Grossly brown tumours are smooth, brown-coloured masses that may have cystic spaces. Histologically, it is impossible to distinguish the brown cell tumour from a reparative granuloma, as they both exhibit multinucleated macrophages with ingrowth of reactive fibrous tissue secondary to microfractures of the thinned bone. Due to the radiographic and histologic similarities between brown tumours, reparative granulomas, and true giant cell tumours, diagnosis of brown tumour relies on finding evidence of hyperparathyroidism. It has been noted that technetium Tc 99m sestamibi scanning, carried out for localization of parathyroid adenoma or hyperplasia, may result in uptake of technetium Tc 99m by the metabolically active brown tumour. Treatment of brown tumour is dependent on the treatment of hyperparathyroidism. Once serum calcium is normalized, the brown tumour may regress, or may require surgical resection. Resection is carried out in the majority of cases to achieve a definitive diagnosis. Recurrence, if the serum calcium is normalized, is extremely unlikely.

Conclusion
Since primary hyperparathyroidism is now regularly diagnosed early in the course of the disease, the finding of brown tumours is becoming rare. It is also exceptionally rare for brown tumour to be the presenting symptom of hyperparathyroidism, in the absence of other symptoms or radiographic findings. The case presented here is therefore of interest because of the unusual finding of advanced bone disease without any other symptoms of hyperparathyroidism. The diagnosis of hyperparathyroidism and brown tumour should be considered in any patient with hypercalcaemia and a destructive expansile bone lesion.

References
Toward the Elimination of Schistosomiasis

Schistosomiasis remains one of the world’s most prevalent diseases. Despite more than a century of control efforts and the introduction of highly effective antischistosomal drug therapy in the 1980s, the disease just will not go away. More than 207 million of the world's poorest people are currently infected with schistosomiasis, which is often a decades-long, chronic inflammatory disorder that is associated with disabling anaemia and undernutrition as well as poor performance in school and at work.

Similarly, until now, preventive chemotherapy has been seen as the most appropriate means of controlling schistosome-related disease in resource-poor areas. Now we are coming to realize that drug delivery may be only a stopgap measure.

Obviously, the elimination of schistosomiasis will be a long-term process requiring a long-term investment, but we must shoulder the necessary extra effort, including long-term planning, intersectoral government coordination, and decades-long commitment. Informed and locally adaptive prevention strategies for long-term control will be necessary.